

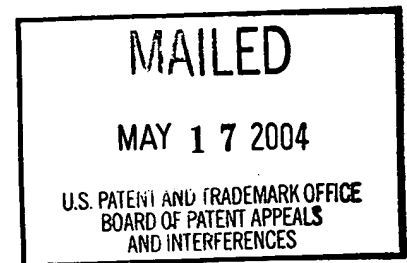
UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte MARIA ALEXANDRA GLUCKSMANN
and MARTIN R. HODGE

Appeal No. 2002-1560¹
Application No. 09/324,465

ON BRIEF



Before WILLIAM F. SMITH, ADAMS and GRIMES, Administrative Patent
Judges.

ADAMS, Administrative Patent Judge.

REMAND

On consideration of the record we find this case is not in condition for a decision on appeal. For the reasons that follow, we remand the application to the examiner to consider the following issues and to take appropriate action.

Claims 2, 9-14, 18-20, 22-30, and 33-37 are pending in this application.

Claims 2, 22 and 25 are illustrative of the subject matter on appeal and are reproduced below:

2. An isolated antibody that selectively binds to a polypeptide having an amino acid sequence selected from the group consisting of:

¹ This appeal is closely related to Appeal No. 2002-1737, Application No. 09/464,685. In this regard, we note that the issue presented for review, as well as the Answer, Brief, and Reply Brief are substantially the same. Accordingly, we have considered these two appeals together.

- (a) the amino acid sequence shown in SEQ ID NO:1;
- (b) the amino acid sequence encoded by the cDNA contained in ATCC Deposit No. PTA-2369;
- (c) the amino acid sequence of an allelic variant of the amino acid sequence shown in SEQ ID NO:1;
- (d) the amino acid sequence of an allelic variant of the amino acid sequence encoded by the cDNA contained in ATCC Deposit No. PTA-2369;
- (e) the amino acid sequence of a sequence variant of the amino acid sequence shown in SEQ ID NO:1, wherein the sequence variant is encoded by a nucleic acid molecule hybridizing to the nucleic acid molecule shown in SEQ ID NO:2 under stringent conditions;
- (f) the amino acid sequence of a sequence variant of the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. PTA-2369, wherein the sequence variant is encoded by a nucleic acid molecule hybridizing under stringent conditions to the cDNA contained in ATCC Deposit No. PTA-2369;
- (g) a fragment of the amino acid sequence shown in SEQ ID NO:1, wherein the fragment comprises at least 12 contiguous amino acids;
- (h) a fragment of the amino acid sequence encoded by the cDNA contained in ATCC Deposit No. PTA-2369, wherein the fragment comprises at least 12 contiguous amino acids;
- (i) the amino acid sequence of the mature receptor polypeptide from about amino acid 6 to about amino acid 359, shown in SEQ ID NO:1;
- (j) the amino acid sequence of the mature polypeptide from about amino acid 6 to about amino acid 359, encoded by the cDNA clone contained in ATCC Deposit No. PTA-2369;
- (k) the amino acid sequence of the transmembrane domain of the polypeptide shown in SEQ ID NO:1, from about amino acid 43 to about amino acid 318;
- (l) the amino acid sequence of the transmembrane domain from about amino acid 43 to about amino acid 318 in the polypeptide encoded by the cDNA contained in ATCC Deposit No. PTA-2369;
- (m) the amino acid sequence of an epitope bearing region of any one of the polypeptides of (a)-(l).

22. A method for identifying a compound that binds to a polypeptide having an amino acid sequence of SEQ ID NO:1, said method comprising the steps of:
- (a) contacting a polypeptide, or a cell expressing said with a test compound; and
 - (b) determining whether the polypeptide binds to the test compound.
25. A method for screening a cell to identify an agent that modulates the expression level or activity of the polypeptide having an amino acid sequence in SEQ ID NO:1 in a cell, said method comprising contacting said cell with an agent and measuring the level or activity of said polypeptide.

The references relied upon by the examiner are:

Berendsen, "A Glimpse of the Holy Grail?" Science, Vol. 282, pp 642-43 (1998)

Galperin et al. (Galperin), "Who's your neighbor? New computational approaches for functional genomics," Nature Biotechnology, Vol. 18, pp. 609-13 (2000)

Attwood² (Attwood 1), "The Babel of Bioinformatics," Science, Vol. 290, pp. 471-73 (2000).

GROUND OF REJECTION

Claims 2, 9-14, 18-20, 22-30, and 33-37 stand rejected under 35 U.S.C. § 101 as lacking utility and § 112, first paragraph, for lack of enablement based on the finding of lack of utility.

BACKGROUND

According to appellants' specification (page 4), "[t]he invention is ... based on the identification of a novel GPCR [G-protein coupled receptor], designated the 2871 receptor. The invention provides isolated 2871 receptor polypeptides

² Attwood is cited for the first time in the Answer (see page 6), cf. Reply Brief, page 5.

including a polypeptide having the amino acid sequence shown in SEQ ID NO 1, or the amino acid sequence encoded by the cDNA deposited as ATCC No. PTA-2369 on August 11, 2000....” As set forth on page 1 of appellants’ specification, “G-protein coupled receptors (GPCRs) constitute a major class of proteins responsible for transducing a signal within a cell.” According to appellants (specification, page 2),

The GPCR protein superfamily can be divided into five families: Family I, receptors typified by rhodopsin and the beta2-adrenergic receptor and currently represented by over 200 unique members...; Family II, the parathyroid hormone/calcitonin/secretin receptor family...; Family III, the metabotropic glutamate receptor family...; Family IV, the cAMP receptor family, important in the chemotaxis and development of D. discoideum ...; and Family V, the fungal mating pheromone receptors such as STE2....

With reference to Figure 2, appellants assert (specification, page 5) that when compared against the Prosite database of protein patterns, the 2871 receptor demonstrated “a high score against the seven transmembrane domain rhodopsin family....” According to appellants (Brief, page 2), “[t]he 2871 receptor shares a high level of sequence similarity with a rhodopsin family GPCR consensus domain and contains a GPCR signature sequence. The 2871 receptor is a member of a family of proteins that are known in the art for their importance as therapeutic targets.” Appellants assert (Reply Brief, page 16), “[t]he 2871 receptor shares a high degree of identity with the rhodopsin family [Family I] of GPCRs This rhodopsin GPCR family includes targets for the treatment of numerous disorders including depression, anxiety, migraine, asthma, hypertension, and cardiovascular disorders.”

While the rejections of record are limited to a discussion of the 2871 polypeptide, we note that no claim on appeal is drawn to the 2871 polypeptide. Instead, the claims on appeal are drawn to (1) an antibody, claim 2; (2) methods and kit for detecting the presence of a polypeptide, claims 9-14; (3) methods of identifying an agent that binds to a polypeptide, claims 18, and 22-24; (4) methods of modulating the activity of a polypeptide, claims 19, 20, 29 and 30; (5) methods for screening a cell to identify an agent that modifies expression or activity of a polypeptide, claims 25-28; and (6) methods of modulating GPCR expression in disease states of a patient, claims 33-37.

DISCUSSION

We agree with appellants (Reply Brief, pages 1-3), that the prosecution history on this record is less than clear. Accordingly, we remand the administrative file to the examiner to address the following issues:

I. Is the 2871 polypeptide a G-protein coupled receptor?

According to the examiner (Paper No. 11, page 3), "applicants have not clearly demonstrated that the cloned nucleic acid and its encoded polypeptide is actually a GPCR as was noted in the utility rejection^[3]." In support of this conclusion, the examiner relies on Berendsen and Galperin.

According to the examiner (Paper No. 9, page 5; Answer, page 4), Berendsen "teaches that 'folding to the stable native state has not yet occurred, and the simulations do not contain any relevant statistics on the process' (page

³ We understand the examiner's reference to the "utility rejection" to be the rejection set forth in Paper No. 9.

643, second column).” Appellants point out, however, that Berendsen is “directed toward predicting the native conformation of a protein of known amino acid sequence, not towards predicting merely activity.” Brief, bridging paragraph, pages 8-9. Stated differently, the Berendsen article is directed to predicting the structure of a protein in its final folded confirmation. While the examiner is correct in that “the activity of any protein or polypeptide is dependent upon its structure” (see Answer, page 8), we fail to understand how Berendsen’s discussion of protein folding applies to appellants’ characterization of the 2871 polypeptide as a member of the rhodopsin family (Family I) of GPCRs based on a comparison of the sequence of 2871 against the Pfam database⁴.

Similarly, we are unable to determine the nexus between the examiner’s reliance on Galperin and the facts of record in this application. According to the examiner (Paper No. 9, page 5; Answer, page 5), Galperin “teach that ‘sequence comparison methods, even the best ones, are of little help when a protein has no homologs in current databases or when all database hits are to uncharacterized gene products’.” The examiner has failed to explain why he believes the 2871 polypeptide has no “homologs in current databases,” and/or why all the database hits for the 2871 polypeptide “are to uncharacterized gene products.” In this regard, we find the examiner’s statement (Answer, page 9), “[a]ppellants have not provided any reasonable correlation between the cloned 2871 polypeptide and the characterized GPCRs as cited in Appendix E [of appellants’ Brief],” to be

⁴ According to appellants (Appeal Brief, page 3), and undisputed by the examiner, “[t]he Pfam database provides a curated collection of well-characterized protein family domains with high quality alignments.”

ambiguous. It is unclear, whether the examiner's use of the term "correlation" means (1) there is no evidence on this record that the 2871 polypeptide is likely to be a member of the rhodopsin family of GPCRs, or (2) that appellants' specification fails to describe the specific activity associated with the 2871 polypeptide? In our opinion, these are two distinct issues.

Apparently believing that his reliance on Berendsen and Galperin was insufficient, the examiner relies on a new reference in the Answer. See Answer, bridging sentence, pages 6-7, wherein the examiner relies on Attwood 1 to bolster his position that protein function cannot be ascertained from analysis of its sequence. In our opinion, the introduction of new evidence in the Answer amounts to a new ground of rejection, which is, prohibited under 37 C.F.R. § 1.193(a)(2). Nevertheless, appellants responded to the examiner's newly cited prior art, by citing a second Attwood⁵ reference. According to appellants (Reply Brief, page 6), Attwood 2 "teaches that while functional prediction methods based on the presence of a single motif may be problematic because matches to single motifs lack biological context ... pattern databases such as Pfam overcome many of the flaws inherent in these single motif-based methods." While the examiner indicated (Paper No. 21) that appellants' Reply Brief "has been noted and entered," the examiner did not indicate whether the evidence attached to the Reply Brief was entered and certainly did not favor this record with a response to appellants' arguments in response to the examiner's newly cited prior art.

⁵ Attwood (Attwood 2), "The quest to deduce protein function from sequence: the role of pattern databases," Int. J. Biochem. Cell Biol., Vol. 32, pp. 139-155 (2000).

For the foregoing reasons, we encourage the examiner to take a step back and reconsider the facts on this record, together with the relevant prior art, to determine whether the evidence of record supports the position that the 2871 polypeptide is a member of the rhodopsin family of GPCRs. In this regard, given the examiner's reliance on a new reference in the Answer, it would appear to be proper to provide appellants with a full and fair opportunity to respond, with supporting evidence, to the examiner's new evidentiary basis for rejecting the claimed invention. Therefore, the examiner should clearly indicate whether the evidence supplied in the Reply Brief has been entered into the record. Then, after reviewing the relevant evidence the examiner should clearly state on this record whether the evidence of record does, or does not, support appellants' assertion that the 2871 polypeptide is a member of the rhodopsin family of GPCRs. If the examiner believes that the evidence of record does not support appellants' assertion, the examiner should clearly point out and explain the deficiency in the evidence.

II. Do GPCRs have a well established and specific utility?

According to the examiner (Paper No. 11, page 3), "applicants do indeed provide multiple well established and specific utilities for a GPCR...." We note that the examiner does not favor the record with a discussion as to what these utilities might be, or whether these utilities apply to the entire GPCR superfamily or merely to a particular subfamily. Nevertheless, this statement taken with the examiner's emphasis (Paper No. 9) on whether the 2871 polypeptide is a GPCR apparently led appellants to characterize the single issue on appeal as hinging

"on whether [a]pplicants have established that the 2871 polypeptide is a GPCR."

See Brief, page 2, Issues. As appellants point out (Reply Brief, page 2), "the [e]xaminer agreed with [a]ppellants' statement of the issues in the Appeal Brief that the single issue was whether 2871 is a GPCR (Examiner's Answer, page 2)."

According to appellants (Reply Brief, page 2), while the examiner agreed with appellants' statement of the issue on appeal, and specifically stated on the record that applicants do indeed provide multiple well established and specific utilities for a GPCR, the examiner "switched horses" in the Answer arguing "that even if [a]pplicants establish 2871 as a GPCR, members of the GPCR family of polypeptides do not have well-established utility." According to the examiner (Answer, page 7),

[i]f, for arguments sake, we accept applicants' assertion that the 2871 polypeptide is a GPCR, the specification still does not provide for a substantial or specific utility since GPCRs are grouped in a very large family of proteins having a multitude of functionally distinct activities as [a]ppellants have admitted in the instantly filed specification and Appendix E. Such activities include I) [rhodopsin and the] beta2 adrenergic receptors, II) parathyroid hormone/calcitonin/secretin receptors, III) metabotropic glutamate receptors, IV) CAMP receptors and V) fungal mating pheromone receptors. Appellants have not associated any particular utility with the 2871 polypeptide other than asserting that it is a GPCR.

It appears that the examiner's position is, assuming arguendo that the 2871 polypeptide is a GPCR, since GPCRs are classified into five distinct families, each having different activities, the utility of the 2871 polypeptide is unclear because appellants do not identify to which family the 2871 polypeptide belongs.

However, as discussed in section I above, appellants appear to have characterized the 2871 polypeptide as a member of the rhodopsin family (Family I) of GPCRs.

For the foregoing reasons, we encourage the examiner to take a step back and reconsider the facts on this record, together with the relevant prior art, to determine whether appellants have provided multiple well-established and specific utilities for a GPCR. After having an opportunity to reconsider the relevant evidence, we encourage the examiner to affirmatively state his findings on this record, together with a well-reasoned analysis of the facts leading to his conclusion. In the event the examiner finds that GPCRs have a well-established or specific utility, the examiner should clearly identify what these utilities are and to which family of GPCRs these utilities apply.

III. Separate analysis for each of appellants' claimed inventions:

As set forth above, the claims on appeal are drawn to (1) an antibody, claim 2; (2) methods and kit for detecting the presence of a polypeptide, claims 9-14; (3) methods of identifying an agent that binds to a polypeptide, claims 18, and 22-24; (4) methods of modulating the activity of a polypeptide, claims 19, 20, 29 and 30; (5) methods for screening a cell to identify an agent that modifies expression or activity of a polypeptide, claims 25-28; and (6) methods of modulating GPCR expression in disease states of a patient, claims 33-37.

Notwithstanding the fact that the claims are drawn to a product, kit and methods, we find no separate discussion of any claim before us on appeal. Instead, the rejections of record are limited to a discussion of the 2871 polypeptide.

Accordingly, if after reconsideration of the record, together with the relevant prior art, the examiner remains of the opinion that the claims are unpatentable, we encourage the examiner to separately discuss the merits of each of appellants' claimed inventions.

IV. Obviousness-type Double Patenting:

The examiner presents two grounds of rejection that according to the examiner (Answer, page 3), "are applicable to the appealed claims." These rejections are under 35 U.S.C. § 101 as lacking utility and § 112, first paragraph, for lack of enablement based on the finding of lack of utility. See Answer, pages 3-5. We note, however, that the examiner indicates that a provisional obviousness-type double patenting rejection should also apply to the claims on appeal. See Answer, bridging paragraph, pages 5-6. According to the examiner (id.), since appellants asserted during prosecution that a terminal disclaimer will be filed upon issuance of a Notice of Allowance, "it is presumed that Appellants will file a terminal disclaimer to obviate the provisional obviousness-type double patenting rejection if the application should receive a favorable disposition from the Board of Patent Appeals and Interferences."

In this regard, we note that the practice of making "provisional" double-patenting rejections based on pending applications has been sanctioned by the courts and by this board. See In re Wetterau, 356 F.2d 556, 148 USPQ 499 (CCPA 1966); Ex parte Karol, 8 USPQ2d 1771 (Bd. Pat. App. Int. 1988). Such rejections are proper even when allowable subject matter has not been identified

in one, or even both, of the conflicting applications. See, e.g., Karol, 8 USPQ2d at 1773-74 (claims in application on appeal stood rejected for obviousness-type double patenting over claims in copending application; rejection affirmed even though both claims on appeal and claims in copending application also stood rejected for obviousness).

On this record, however, the examiner did not present this rejection as "applicable to the appealed claims." Accordingly, this rejection is not properly before us for review. In this regard, we note that according to the Manual of Patent Examining Procedure (MPEP) § 804(I)(B), a "'provisional' double patenting rejection should continue to be made by the examiner in each application as long as there are conflicting claims in more than one application unless that 'provisional' double patenting rejection is the only rejection remaining in one of the applications." Stated differently, the rejection should be repeated in each Office Action entered into the record, so as avoid a procedural withdrawal of the rejection. Paperless Accounting, Inc. v. Bay Area Rapid Transit Sys., 804 F.2d 659, 663, 231 USPQ 649, 651-652 (Fed. Cir. 1986); see also MPEP § 707.07(e) ("In taking up an amended application for action the examiner should note in every letter all the requirements outstanding against the application. Every point in the prior action of an examiner which is still applicable must be repeated or referred to, to prevent the implied waiver of the requirement.").

Accordingly, we encourage the examiner to consider whether the provisional obviousness-type double patenting rejection still applies to the claims on appeal, and whether this rejection should be presented as a “ground of rejection” on appeal. On this point, we note that neither appellants’ Brief, nor Reply Brief comment on the provisional obviousness-type double patenting rejection.

In the event that the obviousness-type double patenting rejection still applies to the claims on appeal, we encourage appellants to take some affirmative action to address the merits of this rejection to avoid an affirmance of the rejection of all claims on appeal on this basis. In this regard, we encourage appellants to consider In re Deters, 515 F.2d 1152, 1157, 185 USPQ 644, 48 (CCPA 1975), and In re Jursich, 410 F.2d 803, 807, 161 USPQ 675 (CCPA 1969), both of which discuss the effect of a terminal disclaimer filed after a decision by the Board.

SUMMARY

For the foregoing reasons, we remand the application to the examiner for further consideration. Upon receipt of the application:

A. We encourage the examiner to affirmatively state on this record whether appellants have, or have not, provided multiple well-established and specific utilities for a GPCR. In the event the examiner finds that GPCRs have a well-established or specific utility, the examiner should clearly identify what these utilities are and to which family of GPCRs these utilities apply.

B. In the event that the examiner finds that the 2871 polypeptide is (i) a GPCR, and (ii) a member of the rhodopsin family of GPCRs, if the examiner remains of the opinion that given the facts on this record, the 2871 polypeptide lacks a patentable utility, the examiner should clearly articulate any such finding on this record specifically addressing both sections (i) and (ii) above.

C. In the event that the examiner believes that the claims are unpatentable, the examiner should separately discuss the merits of each of appellants' claimed inventions.

D. The examiner should determine whether the provisional obviousness-type double patenting rejection still applies to the claims on appeal, and whether this rejection should be presented as a "ground of rejection" on appeal.

We emphasize that for each of the above outlined issues the examiner should favor the record with a clear reasoned analysis of his findings, which includes any relevant supporting evidence.

OTHER ISSUES

While we take no position on the merits of this appeal, in the event of further prosecution, we offer the following guidance to assist the examiner in evaluating the issue of utility.

Initially, we note that it is the examiner who bears the initial burden of showing that a claimed invention lacks patentable utility. See In re Brana, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) ("Only after the PTO

provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility.”).

The seminal decision interpreting the utility requirement of § 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). At issue in Brenner was a claim to “a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced.” Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that “where a claimed process produces a known product it is not necessary to show utility for the product.” Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be “useful,” that “simple, everyday word can be pregnant with ambiguity when applied to the facts of life.” Id. at 529, 148 USPQ at 693. Thus,

[it] is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the “new and useful” phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man's grasp and where little or nothing is wholly beyond the pale of “utility”—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.⁶

⁶ The invention at issue in Brenner was a process, but the Court expressly noted that its holding would apply equally to the patenting of the product produced by the process.” Id. at 535, 148 USPQ at 695-96.

The Court, finding “no specific assistance in the legislative materials underlying § 101,” based its analysis on “the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the other.” Id. at 532, 148 USPQ at 695. The Court concluded that “[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.” Id. at 534-35, 148 USPQ at 695.

The Court considered and rejected the applicant's argument that attenuating the requirement of utility “would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge.” The Court noted that, while there is value to encouraging disclosure, “a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development.” Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not “mean to disparage the importance of contributions to the fund of scientific information short of the invention of something ‘useful,’” and that it was not “blind to the prospect that what now seems without ‘use’ may tomorrow command the grateful attention of the public.” Id. at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because “a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.” Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of § 101's utility requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value “in the furtherance of steroidal research and in the application of steroidal materials to veterinary or medical practice.” Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly “show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests.” Id. at 939, 153 USPQ at 51.

The court held that “nebulous expressions [like] ‘biological activity’ or ‘biological properties’” did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants' affidavit help their case: “the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know ‘how to use’ the compounds to find out in the

first instance whether the compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are.” Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. “There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of ‘useful in research’ or ‘useful as building blocks of value to the researcher’ was recognized, and clearly rejected, by the Supreme Court” in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, in In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in Ziegler claimed priority to a German application filed in 1954. “In the German application, Ziegler disclosed only that solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was ‘plastic-like.’” Id. at 1203, 26 USPQ2d at 1605. “Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility.” Id. The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a rejection based on an intervening reference. See id., 26 USPQ2d at 1606. “[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at

the time of the filing of the German application; but in that application Ziegler had not yet gotten there.” Id., 26 USPQ2d at 1605.

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in Jolles claimed pharmaceutical compositions that were disclosed to be useful in treating acute myeloblastic leukemia. See id. at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were “well recognized in the art as valuable for use in cancer chemotherapy.” Id., 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one was effective in treating humans. See id. at 1323-24, 206 USPQ at 887-88. The court noted that the data derived from the mouse model were “relevant to the treatment of humans and [were] not to be disregarded,” id. at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. See id. at 1327-28, 206 USPQ at 891.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in vivo testing (as in Jolles) was not necessarily required to show utility in the pharmaceutical context. The Cross court stated that “[it] is axiomatic that an invention cannot be considered ‘useful,’ in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious.” Id. at 1044, 224 USPQ at 742 (citing Brenner v. Manson). The court “perceive[d] no

insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question.” Id. at 1051, 224 USPQ at 748. Successful in vitro testing could provide an immediate benefit to the public, by “marshal[ing] resources and direct[ing] the expenditure of effort to further in vivo testing of the most potent compounds . . . , analogous to the benefit provided by the showing of an in vivo utility.” Id. On the facts of that case – successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds – the court held that in vitro activity was sufficient to meet the requirements of § 101. See id.

The Federal Circuit confirmed in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in Brana was a group of compounds disclosed to have antitumor activity. See id. at 1562, 34 USPQ2d at 1437-38. The specification disclosed that the claimed compounds had higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. See id., 34 USPQ2d at 1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from Brenner and its progeny. First, § 101's requirement that an invention be "useful" is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every "use" that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy § 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk,

376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best . . . on the way to discovering a practical utility for polypropylene at the time of the filing," but not yet there. Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

In this case, the examiner found the specification "does not provide any evidence or guidance suggesting the claimed protein's activity or that mis-expression of the claimed proteins are involved in any particular activity or disease state." Answer, bridging paragraph, pages 3-4. In response, appellants assert (Reply Brief, page 15), with reference to Stadel⁷, that

[t]hose of skill in the art recognize that the identification of a novel member of the G-protein coupled receptor family provides an immediate benefit. In addition to serving as reagents and targets in the diagnosis and treatment of 2871-mediated disorders as described in the specification on page 48 et seq., all members of the GPCR protein family have utility in selectivity screening of candidate drugs that target GPCRs.

In addition, appellants assert (Reply Brief, page 18), "[w]hile the [e]xaminer's assertion of lack of utility may reflect the thinking of the pre-genomics era, it does not accurately describe the current state of the art in drug discovery." With reference to Stadel, appellants assert (Reply Brief, bridging paragraph, pages 18-19, citations omitted),

The advances in molecular biology have led to what those in the art consider a "paradigm shift" in the way research and drug discovery is conducted. . . . In this new paradigm, the starting point in the process is the identification of new members of gene families such

⁷ Stadel et al. (Stadel), "Orphan G protein-coupled receptors: a neglected opportunity for pioneer drug discovery," TIPS, Vol. 18, pp. 430-437 (1997).

as the GPCR superfamily by “computational or bioinformatic methodologies.” ... “Once new member of the GPCR superfamily are identified, the recombinantly expressed receptors are used in functional assays to search for the associated novel ligands. The receptor-ligand pair are then used for compound bank screening to identify a lead compound that, together with the activating ligand, is used for biological and pathophysiological studies to determine the function and potential therapeutic value of a receptor antagonist (or agonist) in ameliorating a disease process....”

Thus, appellants conclude (Reply Brief, page 19),

in the molecular biology field of the present invention, the discovery of a novel sequence is the key step, or “first link” of Cross [F.2d at 1051, 224 USPQ at 748] ... (holding that “[w]e perceive no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vivo testing, may establish a practical utility for the compound in question.”)

We recognize that Stadel teach (bridging paragraph, pages 433- 434), “reverse molecular pharmacology” represents a new paradigm in the way research and drug discovery is conducted, wherein the starting point in the process is the identification of new members of gene families such as the GPCR superfamily. However, Stadel also teach (page 434, column 1), the very next step is “to search for the associated novel ligands.” Stadel characterizes this step as “ligand fishing.” See Stadel, page 434, Figure 2. As appellants recognize (Reply Brief, page 19), once a ligand is identified, “[t]he receptor-ligand pair are then used for compound bank screening to identify a lead compound that, together with the activating ligand, is used for biological and pathophysiological studies to determine the function and potential therapeutic value of a receptor antagonist (or agonist) in ameliorating a disease process.” According to Stadel, (page 434, column 1), “[o]nce a link with a disease is finally identified, an appropriate compound can be advanced for clinical study.”

We note, however, that Stadel teach (page 434, bridging paragraph, columns 1-2), the starting material, e.g., a receptor obtained by computational or bioinformatic methodologies is “simply an orphan receptor of unknown function, with no apparent relationship to a disease indication.” Without knowing any further information in regard to function or a relationship to a disease indication, it appears that this starting material provides the barest information in regard to utility and may be viewed to be at the lower end of the utility spectrum. At the high end of the utility spectrum would be information obtained from identifying the receptor’s ligand, using the receptor-ligand pair to screen compounds and determining the function and potential therapeutic value of a receptor antagonist (or agonist) in ameliorating a disease process (e.g., establishing a link with a disease). Stadel characterizes this as the “potential reward of using this [reverse molecular pharmacology] approach,” wherein “resultant drugs naturally will be pioneer or innovative discoveries, and a significant proportion of these unique drugs may be useful to treat diseases for which existing therapies are lacking or insufficient.” See Stadel, page 434, bridging paragraph, columns 1-2.

On this record, we leave to the examiner to establish a factual basis as to where appellants’ claimed invention falls along this utility spectrum, and whether or not the claimed invention has a well-established or substantial utility. Again, a “starting material” for a drug discovery effort that is an orphan receptor of unknown function, with no apparent relationship to a disease indication may very

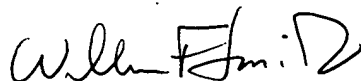
well represent the lowest end of the spectrum, i.e., an insubstantial use. Such a "starting material" would distinguish the facts of this case from the facts in Cross, F.2d at 1051, 224 USPQ at 748,

where the Japanese priority application discloses an in vitro utility, i.e., the inhibition of thromboxane synthetase in human or bovine platelet microsomes, and where the disclosed in vitro utility is supplemented by the similar in vitro and in vivo pharmacological activity of structurally similar compounds, i.e., the parent imidazole and 1-methylimidazole compounds, we agree with the Board that this in vitro utility is sufficient to comply with the practical utility requirement of §101.

FURTHER PROCEEDINGS

We authorize the examiner to file a Supplemental Examiner's Answer to address the issues set forth herein. If a Supplemental Examiner's Answer is filed, Appellants are entitled to file a Supplemental Reply Brief. See 37 CFR § 1.193(b)(1).

REMANDED



William F. Smith
Administrative Patent Judge



Donald E. Adams
Administrative Patent Judge



Eric Grimes
Administrative Patent Judge

)
)
)
)
)
) BOARD OF PATENT
)
) APPEALS AND
)
) INTERFERENCES
)
)
)

INTELLECTUAL PROPERTY GROUP
MILLENNIUM PHARMACEUTICALS, INC
75 SIDNEY STREET
CAMBRIDGE MA 02139

BOARD OF APPEALS

U.S. DEPARTMENT OF COMMERCE PATENT OFFICE		DATE OF MEMORANDUM <u>5-17-04</u>
SERIAL NUMBER <u>591324, 4165</u>	APPEAL NUMBER <u>2062-1560</u>	
APPLICATION FILING DATE <u>0-2-99</u>		
FORM PTO-262 (5/95)		
EXAMINER'S DISPOSITION OF APPEAL		
To:	From:	
Clerk, Board of Appeals	Group Art Unit <u>1642</u>	
GROUP: Please detach and forward to Board of Appeals promptly, but ONLY if the appeal is suspended or no longer pending.		
The Examiner has:		
<input checked="" type="checkbox"/> 1. Withdrawn the final rejection and		
<input type="checkbox"/> a. allowed all the claims		
<input checked="" type="checkbox"/> b. made a new rejection and reopened the prosecution		
<input type="checkbox"/> c. other		
<input type="checkbox"/> 2. Maintained the final rejection, but has		
<input type="checkbox"/> a. instituted an interference which cannot proceed concurrently with the appeal (Note M.P.E.P. 1205)		
<input type="checkbox"/> b. other		
<input type="checkbox"/> 3. The application is now abandoned.		
<u>08/23/04</u> (Date signed)		<u>GARY B NICKOL</u> (Signed)